

**Amendments to the Claims**

Claims 1-47 (Cancelled)

48. (New) A method for detecting an interaction between a first membrane bound protein or part thereof and a second protein or part thereof, which is either membrane bound or soluble, the method comprising:

- (a) providing a host cell containing at least one detectable gene (reporter gene) having a binding site for a transcriptional activator, such that the detectable gene expresses a detectable product when the detectable gene is transcriptionally activated;
- (b) providing, as part of a bait vector, a first chimeric gene under the control of a promoter, said first chimeric gene being expressed in said host cell and coding *inter alia* for a first membrane protein or part thereof which gene is attached to the DNA-sequence of a first module encoding *inter alia* a first protein sequence involved in intracellular protein degradation and a transcriptional activator, said first protein or part thereof to be tested whether it can interact with a second protein or part thereof;
- (c) providing, as a part of a prey vector, a second chimeric gene under the control of a promoter that can be expressed in said host cell, the second chimeric gene coding *inter alia* for a second protein or part thereof which is either membrane bound or soluble and which gene is attached to the DNA sequence of a second module encoding *inter alia* a second protein sequence involved in intracellular protein degradation;
- (d) introducing the bait vector and the prey vector into the host cell such that an interaction between the expressed first and second proteins and/or their parts can take place, which interaction leads to an interaction of the first protein sequence of the first module and the second protein sequence of the second module which interaction in turn leads to activation of an intracellular protease and proteolytic separation of the transcriptional activator, wherein both the bait vector and the prey vector can be maintained episomally; and
- (e) determining whether the detectable gene of the host cell has been activated by the transcriptional activator.

49. (New) The method according to claim 48, wherein the host cell is a yeast, a bacterium or a mammalian cell.

50. (New) The method according to claim 49, wherein the yeast is *Saccharomyces pombe* or *Saccharomyces cerevisiae*.

51. (New) The method according to claim 48, wherein the detectable gene is activated by an activator comprising a short tagging module.

52. (New) The method according to claim 48, wherein the detectable gene is activated by the artificial transcriptional activator protein A-LexA-V16 (PLV).

53. (New) The method according to claim 48, wherein the first protein sequence comprises a C-terminal portion of ubiquitin (Cub) or a mutant thereof (CbM) and the second protein sequence comprises an N-terminal portion of ubiquitin (Nub) or a mutant thereof (NbM).

54. (New) The method according to claim 48, wherein the DNA-sequence coding for the first membrane protein is selected from the group consisting of any bacterial membrane protein, any viral membrane protein, any oncogene-encoded membrane protein, any growth factor receptor or any eukaryotic membrane protein, or parts thereof.

55. (New) The method according to claim 48, wherein the second membrane protein or the soluble protein, or part thereof, is encoded by a plasmid library.

56. (New) The method according to claim 48, wherein the first membrane protein is a soluble protein attached artificially to the membrane.

57. (New) A kit for detecting binding between a first membrane bound protein or part thereof and a second protein or part thereof which is either membrane bound or soluble comprising:

- (a) a host cell containing at least one detectable gene (reporter gene) having a binding site for a transcriptional activator, such that the detectable gene expresses a detectable product when the detectable gene is transcriptionally activated;
- (b) a first vector (bait), which can be maintained episomally, comprising a first site that can receive a first nucleic acid coding for a first membrane protein or

- part thereof such that when the first nucleic acid is inserted it becomes attached to the DNA sequence of a first module encoding *inter alia* a first protein sequence involved in intracellular protein degradation, the first module further comprising a nucleic acid for a transcriptional activator and a promoter;
- (c) a second vector (prey), which can be maintained episomally, comprising a second site that can receive a second nucleic acid coding for a second membrane protein or a soluble protein or part thereof such that when the second nucleic acid is inserted it becomes attached to the DNA sequence of a second module encoding *inter alia* a sequence protein sequence involved in intracellular protein degradation, wherein the second module further comprises a promoter; and optionally
- (d) a plasmid library encoding second proteins or parts thereof.

58. (New) The kit according to claim 57, wherein the host cell is a yeast, a bacterium or a mammalian cell.

59. (New) The kit according to claim 58, wherein the yeast is *Saccharomyces pombe* or *Saccharomyces cerevisiae*.

60. (New) The kit according to claim 57, wherein the detectable gene can be activated by an activator comprising a short tagging module.

61. (New) The kit according to claim 57, wherein the detectable gene can be activated by the artificial transcriptional activator protein A-LexA-V16 (PLV).

62. (New) The kit according to claim 57, wherein the first protein sequence contains Cub or CbM and the second protein sequence contains Nub or NbM.

63. (New) The kit according to claim 57, wherein the promoter is selected from the group consisting of ADH promoter, CYC1 promoter and TEF1 promoter.

64. (New) The kit according to claim 57, wherein the DNA sequence coding for the first membrane protein is derived from any bacterial membrane protein, any viral membrane protein, any oncogene-encoded membrane protein, any growth factor receptor or any eukaryotic membrane protein, or parts thereof.

65. (New) The kit according to claim 57, wherein the DNA sequence coding for the second protein is contained in a plasmid library.

66. (New) A vector useful as a bait vector in the method of claim 1, wherein the vector comprises the following elements:

- (a) a selection marker for propagation of the vector in *E. coli*;
- (b) an origin of replication which allows propagation of the vector in *E. coli*;
- (c) a further selection marker for propagation of the vector in yeast;
- (d) an origin of replication which allows propagation of the vector in yeast; and
- (e) an expression cassette comprising the following elements:
  - (i) a promoter element;
  - (ii) a nucleic acid sequence encoding a leader selected from a signal sequence derived from a yeast integral membrane protein and a signal sequence, which confers fatty acid modification;
  - (iii) a nucleic acid sequence encoding Cub or CbM;
  - (iv) a nucleic acid sequence encoding a DNA binding protein; and
  - (v) a nucleic acid sequence encoding a transcriptional activator.

67. (New) A host cell containing the vector of claim 66.

68. (New) A method of identifying a potentially pharmaceutically active agent, which method comprises using the kit of claim 57 to screen an agent for the ability to interfere with protein-protein interaction, whereupon the ability to interfere with protein-protein interaction is indicative of the agent being potentially pharmaceutically active.

69. (New) A method for providing a compound that can interfere with protein/protein interaction, which method comprises:

- (a) providing a host cell according to claim 67, the bait and prey polypeptides being selected such that they interact when expressed;
- (b) incubating the host cell in the presence and absence of the compound(s) to be tested;
- (c) measuring the difference in reporter gene expression between the incubation containing the compound(s) to be tested and the incubation free of the compound(s) to be tested; and optionally

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(U.S. National Phase of PCT/EP03/03287)

- (d) purifying or synthesizing the compound that can interfere with protein-protein interaction.